

0515/71131-PCT

JPW

## PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To:  
 JOHN P. WHITE  
 COOPER & DUNHAM LLP  
 1185 AVENUE OF THE AMERICAS  
 NEW YORK, NY 10036

FEB - 7 2006

## PCT

NOTIFICATION OF TRANSMITTAL OF  
 THE INTERNATIONAL SEARCH REPORT AND  
 THE WRITTEN OPINION OF THE INTERNATIONAL  
 SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

02 FEB 2006

Applicant's or agent's file reference 71131-PCT/JP	Date of mailing (day/month/year)
International application No. PCT/US04/42504	FOR FURTHER ACTION See paragraphs 1 and 4 below International filing date (day/month/year) 17 December 2004 (17.12.2004)
Applicant THE TRUSTEES OF COLUMBIA UNIVERSITY IN THE CITY OF	Article 19 Amend: 4/2/06

1.  The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

**Filing of amendments and statement under Article 19:** *IDS Based on Search: 5/2/06*  
 The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

**When?** The time limit for filing such amendments is normally two months from the date of transmittal of the international search report.

**Where?** Directly to the International Bureau of WIPO, 34 chemin des Colombettes  
 1211 Geneva 20, Switzerland, Facsimile No.: +41 22 740 14 35

For more detailed instructions, see the notes on the accompanying sheet.

2.  The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.

3.  With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.  
 no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. Reminders

Shortly after the expiration of 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

Within 19 months from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later); otherwise, the applicant must, within 20 months from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of 30 months (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

Name and mailing address of the ISA/ US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer Terra C. Gibbs Telephone No. 571-272-0564
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Form PCT/ISA/220 (January 2004)

(See notes on accompanying sheet)

# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 71131-PCT/JP	<b>FOR FURTHER ACTION</b> <small>see Form PCT/ISA/220 as well as, where applicable, item 5 below.</small>	
International application No. PCT/US04/42504	International filing date (day/month/year) 17 December 2004 (17.12.2004)	(Earliest) Priority Date (day/month/year) 17 December 2003 (17.12.2003)
Applicant THE TRUSTEES OF COLUMBIA UNIVERSITY IN THE CITY OF		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 9 sheets.



It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the Report**

a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.



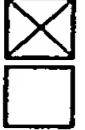
The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b.  With regard to any nucleotide and/or amino acid sequence disclosed in the international application, see Box No. I.

2.  Certain claims were found unsearchable (See Box No. II)

3.  Unity of invention is lacking (See Box No. III)

4. With regard to the title,



the text is approved as submitted by the applicant.



the text has been established by this Authority to read as follows:

5. With regard to the abstract,



the text is approved as submitted by the applicant.



the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the drawings,

a. the figure of the drawings to be published with the abstract is Figure No. \_\_\_\_\_



as suggested by the applicant.



as selected by this Authority, because the applicant failed to suggest a figure.



as selected by this Authority, because this figure better characterizes the invention.



none of the figures is to be published with the abstract.

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/42504

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C12Q 1/68; A01N 43/04; C07H 21/04; A61K 31/07  
 US CL : 435/6, 91.1, 325, 375; 536/23.1, 24.3, 24.33, 24.5

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/6, 91.1, 325, 375; 536/23.1, 24.3, 24.33, 24.5

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
 Please See Continuation Sheet

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	FRENDO et al. Involvement of connexin 43 in human trophoblast cell fusion and differentiation. Journal of Cell Science, 2003 Vol. 116:3413-3421, see Abstract, Table 1, page 3415, first column, and Figure 4.	1-4, 6, 8, 10, 11-14, and 20-23
X	PERACCHIA et al. Is the Voltage Gate of Connexins CO2-sensitive? Cx45 Channels and Inhibition of Calmodulin Expression. Journal of Membrane Biology, 2003 Vol. 195:53-62, see Abstract, page 2045, first column, and Figure 3.	1-4, 6, 8, 10-12, 16, and 20-23
X	LI et al. Inhibiting Gap Junctional Intercellular Communication Alters Expression of Differentiation Markers in Osteoblastic Cells. Bone, 1999 Vol. 23, pages 661-666, see Figure 1.	1-4, 6, 11-14, and 20-23
X	VALIJUNAS et al. Gap junction channels formed by coexpressed connexin40 and connexin43. Am J. Physiol. Heart Circ Physiol., 2001 Vol. 281:H1675-H1689, see Abstract, page H1677, first column, and Table 1, and Figure 6.	1-3, 6, 10-15, and 19-23



Further documents are listed in the continuation of Box C.



See patent family annex.

Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E" earlier application or patent published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O" document referring to an oral disclosure, use, exhibition or other means		
"P" document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search

07 June 2005 (07.06.2005)

Date of mailing of the international search report

02 FEB 2006

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US  
 Commissioner for Patents  
 P.O. Box 1450  
 Alexandria, Virginia 22313-1450

Facsimile No. (703) 305-3230

Authorized officer

Terra C. Gibbs

Telephone No. 571-272-0564

**INTERNATIONAL SEARCH REPORT**

International application No. PCT/US04/42504
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**C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	REED et al. Molecular Cloning and Functional Expression of Human Connexin37, an Endothelial Cell Gap Junction Protein. Journal of Clinical Investigation, 1993 Vol. 91, pages 997-1004, see Abstract and Figure 8.	1-3, 6, 10-12, 18, and 20-23
Y	ELBASHIR et al. Duplexes of 21-nucleotide RNAs mediate RNA interference in cultured mammalian cells. Nature, 2001 Vol. 411, pages 494-498, see entire article.	1-23

**INTERNATIONAL SEARCH REPORT**

International application No.  
PCT/US04/42504

Continuation of B. FIELDS SEARCHED Item 3:  
Medline, NPL, STN Databases: CaPlus, EmBase, CancerLit, WEST  
search terms: antisense, siRNA, small interfering RNA, gap junction, connexin